REMARKS

The Official Action dated August 15, 2001 has been carefully considered. Accordingly, the changes presented herewith, taken with the following remarks, are believed sufficient to place the present application in condition for allowance. Reconsideration is respectfully requested.

By the present Amendment, claims 8 and 10 are amended to clarify the enhancer elements by removing reference to "remaining enhancer elements." Claim 10 as amended is believed to properly correspond with claim 9 from which it depends. Claims 5, 15, 19 and 44 are amended to clarify the limitations therein, generally in accord with the Examiner's suggestions. Finally, claims 27 and 30 are amended to clarify that the enhancer element is incorporated "within" the structural gene by "transfection," in accordance with the teachings in the specification. A Version With Markings Showing Changes Made is attached. It is believed that these changes do not involve any introduction of new matter, whereby entry is believed to be in order and is respectfully requested.

In the Official Action, the Examiner objected under 35 U.S.C. §132 to the Amendment filed May 22, 2001 on the basis that the Amendment introduced new matter in the disclosure. The Examiner asserted that the added material not supported by the original disclosure was in claims 8 and 10.

This objection is traversed. However, to expedite prosecution, Applicants have amended claims 8 and 10 to omit reference to remaining enhancer elements. It is believed that claims 8 and 10 now recite expression vectors fully supported by the specification as originally filed, whereby the objection has been overcome. Reconsideration is respectfully requested.

Claims 1, 2, 5, 7-11, 15-17, 19-21, 23-32, 34-36, 39-42, 44-50, 52 and 53 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. With respect to claims

1, 2, 19-21, 39, 40, 49, 51 and 52, the Examiner asserted that the respective preambles of claims 1 and 19 were in conflict with the body of the claims and it was unclear where the DNA construct is incorporated. With respect to claims 5, 7-11, 15-17, 23-26, 34-36, 50 and 53, the Examiner asserted that these claims are indefinite because the enhancer element alone is not hormone responsive but must be incorporated into a DNA construct to be responsive. With respect to claims 44 and 45, the Examiner asserted that these claims are indefinite because the arrangement of the genetic elements is not specified.

This rejection is traversed with respect to present claims 1, 2, 5, 7-11, 15-17, 19-21, 23-32, 34-36, 39-42, 44-50, 52 and 53, and reconsideration is respectfully requested. More particularly, claims 1 and 19 recite methods of enhancing the transcription of a gene in a DNA construct, which methods include providing a DNA construct comprising a structural gene, a promoter upstream of the structural gene, and an enhancer element (claim 1) or a defined nucleotide sequence (claim 19) upstream of the promoter. In addition, claims 1 and 19 recite that the DNA construct is incorporated into the genome of a host cell. Claims 5 and 15 recite that the enhancer element is responsive when used in a DNA construct transfected into the genome of a host cell. Claim 44 recites the arrangement of the genetic elements as a promoter, "a structural gene downstream from said promoter" and six repeats of an enhancer element "upstream from said promoter". Finally, Applicants note that claims 8 -11, 16, 17 and 34 do not recite hormone responsiveness, and claim 51 was previously cancelled from the application.

It is therefore submitted that all of claims 1, 2, 5, 7-11, 15-17, 19-21, 23-32, 34-36, 39-42, 44-50, 52 and 53 are definite and the rejection under 35 U.S.C. §112, second paragraph, has been overcome. Reconsideration is respectfully requested.

Claims 19, 20 and 49 were rejected under 35 U.S.C. §102(b) as being anticipated by Yoon et al (1990). The Examiner asserted that the constructs described by Yoon et al are of

the type described in the claims. Specifically, the Examiner asserted that the minimal sequence does not need to be recognized or taught because the enhancer element used in Yoon et al consists of flanking sequences and the nucleotide sequence TTCTGAGAA.

As will be set forth below, Applicants submit that the methods defined by the present claims 19, 20 and 49 are not anticipated by Yoon et al. Accordingly, this rejection is traversed and reconsideration is respectfully requested.

Claim 19 recites an in vitro method of enhancing the transcription of a gene in a DNA construct. The method comprises providing a DNA construct comprising a structural gene and a promoter upstream of the structural gene, providing the DNA construct with the nucleotide sequence consisting of TTCTGAGAA upstream of the promoter, transfecting a eukaryotic host cell to incorporate the DNA construct into the genome of the host cell, and exposing the DNA construct to a hormone selected from the group consisting of lactogenic hormones, somatogenic hormones and mixtures thereof.

Anticipation under 35 U.S.C. §102(b) requires the disclosure in a single prior art reference of each element of the claims under consideration, *Alco Standard Corp. v. TVA*, 1 U.S.P.Q.2d 1337, 1341 (Fed. Cir. 1986). While the construct of Yoon et al may include an enhancer element including the nucleotide sequence TTCTGAGAA, with flanking sequences as noted by the Examiner, Applicants find no teaching or suggestion by Yoon et al of a method wherein a DNA construct is provided with the nucleotide sequence consisting of TTCTGAGAA. Rather, Yoon et al provide a larger nucleotide sequence. Thus, Yoon et al do not disclose each element of the present claims and therefore do not anticipate these claims.

It is therefore submitted that the methods defined by claim 19, and claims 20 and 49 dependent thereon, are not anticipated by Yoon et al, and that the rejection under 35 U.S.C. §102 has been overcome. Reconsideration is respectfully requested.

Claims 27-32 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lindquester et al (1989). The Examiner asserted that Lindquester et al need not disclose the function of the sequence because the claims are directed to compositions that include the sequence.

However, as will be set forth in detail below, Applicants submit that the respective expression vectors and DNA constructs defined by claims 27-32 are nonobvious over and patentably distinguishable from the teachings of Lindquester et al. Accordingly, this rejection is traversed and reconsideration is respectfully requested.

More specifically, as defined by claim 27, the expression vector comprises a structural gene encoding a protein, a promoter, and at least one enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA. The enhancer element is incorporated within the structural gene by transfection. Claim 30 is directed to a DNA construct comprising a promoter, a structural gene, and at least one enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA. The enhancer element is incorporated within the structural gene by transfection.

In contrast, Lindquester et al describe their study of avian tropomyosin gene expression. As noted by the Examiner, Lindquester et al disclose that the avian tropomyosin gene includes the sequence TTCTGAGAA located in one of the introns, specifically at position 18602 of Figure 1 on page 2105, and that a genomic clone containing tropomyosin gene was isolated from a quail DNA genomic library.

However, Applicants find no teaching or suggestion by Lindquester et al of an expression vector as defined in claim 27 or a DNA construct as defined in claim 30 comprising, inter alia, a structural gene, a promoter, and at least one enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA, particularly wherein the enhancer element is incorporated within the structural gene by transfection. Moreover, the

mere teaching by Lindquester et al of the avian tropomyosin gene including the nucleotide sequence TTCTGAGAA, without further teaching, suggestion or recognition of the ability of the nucleotide sequence to act as an enhancer element, provides no teaching or suggestion to one of ordinary skill in the art to produce either an expression vector or a DNA construct as recited in claims 27 and 30, wherein the enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA is incorporated within the structural gene by transfection.

References relied upon to support a rejection under 35 U.S.C. §103 must provide an enabling disclosure, i.e., they must place the claimed invention in the possession of the public, *In re Payne*, 203 U.S.P.Q. 245 (CCPA 1979). Lindquester's disclosure of the avian tropomyosin gene including the nucleotide sequence TTCTGAGAA does not place either the expression vector of claim 27 or the DNA construct of claim 30 comprising, inter alia, an enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA incorporated within the structural gene by transfection in the possession of the public. Similarly, Lindquester et al's disclosure of the avian tropomyosin gene including the nucleotide sequence TTCTGAGAA does not provide an enabling disclosure of either the expression vector of claim 27 or the DNA construct of claim 30 which comprise, inter alia, the enhancer element incorporated within the structural gene by transfection. Thus, Lindquester et al do not support a rejection of claims 27 and 30 under 35 U.S.C. §103. It is therefore submitted that the expression vector as defined by claim 27 and the DNA construct defined by claim 30 are nonobvious over and patentably distinguishable from Lindquester et al, whereby the rejection of claims 27-32 under 35 U.S.C. §103 has been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the Examiner's rejections under 35 U.S.C. §§ 102, 103 and 112, second paragraph, and places the present

application in condition for allowance. Reconsideration and an early allowance are requested.

Respectfully submitted,

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VERSION WITH MARKINGS SHOWING CHANGES MADE

In the Claims:

Claims 1, 5, 8, 10, 15, 19, 27, 30 and 44 are amended as follows:

1. (Sixth Amendment) An in vitro method of enhancing the transcription of a gene in a DNA construct when the DNA construct is incorporated into the genome of a eukaryotic host cell, [said DNA construct comprising a structural gene for a desired protein or polypeptide and a gene promoter upstream of the structural gene, the method comprising the steps of:]

(a) providing a [the] DNA construct comprising a structural gene for a desired protein or polypeptide, a gene promoter upstream of the structural gene, and [with] six copies of an enhancer element upstream of the promoter;

(b) transfecting the eukaryotic host cell to incorporate the DNA construct into the genome of the host cell;[,] and

(c) exposing the DNA construct to a hormone selected from the group consisting of lactogenic hormones, somatogenic hormones and mixtures thereof;

wherein the enhancer element comprises the nucleotide sequence TTCTGAGAA, with the proviso that the nucleotide sequence does not contain the DNA sequence of nucleotide sequence SEQ ID NO:1, and wherein the enhancer element is responsive to both lactogenic hormones and somatogenic hormones.

5. (Fifth Amendment) An enhancer element which when used in a DNA construct for transfection of a eukaryotic host cell is responsive to hormonal stimuli, said enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA, wherein the enhancer element is responsive to both lactogenic hormones and somatogenic hormones when used in a DNA construct transfected into the genome of a eukaryotic host cell.

8. (Fourth Amendment) An expression vector comprising a structural gene encoding a desired protein or polypeptide and a promoter, wherein the vector further comprises six enhancer elements, and further wherein at least one of the enhancer elements consists essentially of the nucleotide sequence TTCTGAGAA [and the remaining enhancer elements comprise the nucleotide sequence TTCTGAGAA].

10. (Fifth Amendment) The expression vector according to claim 9, wherein [at least one of the remaining] the enhancer [elements is] element comprises at least one copy of the nucleotide sequence SEQ ID NO:1.

15. (Twice Amended) The enhancer element of claim 5 wherein the enhancer element is responsive to signals generated from both growth hormone and prolactin receptors when used in a DNA construct transfected into the genome of a eukaryotic host cell.

19. (Fourth Amendment) An in vitro method of enhancing the transcription of a gene in a DNA construct,

(a) providing a DNA construct comprising a structural gene and a promoter upstream of the structural gene, [the method comprising:]

(b) [(a)] providing the DNA construct with [at least one enhancer element consisting of] the nucleotide sequence consisting of TTCTGAGAA upstream of the promoter;

(c) [(b)] transfecting a eukaryotic host cell [wherein transcription can occur] to incorporate the DNA construct into the genome of the host cell;[,] and

(d) [(c)] exposing the DNA construct to a hormone selected from the group consisting of lactogenic hormones, somatogenic hormones and mixtures thereof.

27. (Fourth Amendment) An expression vector comprising a structural gene encoding a protein, a promoter, and at least one enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA, wherein the enhancer element is incorporated [with] within the structural gene by [fusion] transfection.

30. (Third Amendment) A DNA construct comprising a promoter, a structural gene, and at least one enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA, wherein the enhancer element is incorporated [with] within the structural gene by [fusion] transfection.

44. (Third Amendment) An isolated DNA construct comprising [a structural gene,] a promoter, a structural gene downstream from said promoter, and six repeats of an enhancer element upstream from said promoter, wherein the enhancer element consists essentially of the sequence TTCTGAGAA.